

SEQUENCE LISTING

<110> VERTEX PHARMACEUTICALS, INC. et al.

<120> CRYSTAL STRUCTURES OF JNK-INHIBITOR COMPLEXES AND
BINDING POCKETS THEREOF

<130> VPI/02-01PCT

<140>

<141>

<150> 60/348,002

<151> 2002-01-11

<160> 7

<170> PatentIn Ver. 2.1

<210> 1

<211> 422

<212> PRT

<213> Homo sapiens

<400> 1

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ser | Leu | His | Phe | Leu | Tyr | Tyr | Cys | Ser | Glu | Pro | Thr | Leu | Asp | Val |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Ile | Ala | Phe | Cys | Gln | Gly | Phe | Asp | Lys | Gln | Val | Asp | Val | Ser | Tyr |
| | | | 20 | | | | | 25 | | | | | 30 | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Ala | Lys | His | Tyr | Asn | Met | Ser | Lys | Ser | Lys | Val | Asp | Asn | Gln | Phe |
| | | 35 | | | | | 40 | | | | | 45 | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Ser | Val | Glu | Val | Gly | Asp | Ser | Thr | Phe | Thr | Val | Leu | Lys | Arg | Tyr |
| | 50 | | | | | 55 | | | | | 60 | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Asn | Leu | Lys | Pro | Ile | Gly | Ser | Gly | Ala | Gln | Gly | Ile | Val | Cys | Ala |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Tyr | Asp | Ala | Val | Leu | Asp | Arg | Asn | Val | Ala | Ile | Lys | Lys | Leu | Ser |
| | | | 85 | | | | | | 90 | | | | | 95 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Pro | Phe | Gln | Asn | Gln | Thr | His | Ala | Lys | Arg | Ala | Tyr | Arg | Glu | Leu |
| | | 100 | | | | | | 105 | | | | | 110 | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Leu | Met | Lys | Cys | Val | Asn | His | Lys | Asn | Ile | Ile | Ser | Leu | Leu | Asn |
| | 115 | | | | | | 120 | | | | | 125 | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Phe | Thr | Pro | Gln | Lys | Thr | Leu | Glu | Glu | Phe | Gln | Asp | Val | Tyr | Leu |
| | 130 | | | | | 135 | | | | | 140 | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Met | Glu | Leu | Met | Asp | Ala | Asn | Leu | Cys | Gln | Val | Ile | Gln | Met | Glu |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Asp | His | Glu | Arg | Met | Ser | Tyr | Leu | Leu | Tyr | Gln | Met | Leu | Cys | Gly |
| | | | 165 | | | | | | 170 | | | | | 175 | |

Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp Leu Lys Pro
 180 185 190
 Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe
 195 200 205
 Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr Pro Tyr Val
 210 215 220
 Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly Met Gly Tyr
 225 230 235 240
 Lys Glu Asn Val Asp Ile Trp Ser Val Gly Cys Ile Met Gly Glu Met
 245 250 255
 Val Arg His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp
 260 265 270
 Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu Phe Met Lys
 275 280 285
 Lys Leu Gln Pro Thr Val Arg Asn Tyr Val Glu Asn Arg Pro Lys Tyr
 290 295 300
 Ala Gly Leu Thr Phe Pro Lys Leu Phe Pro Asp Ser Leu Phe Pro Ala
 305 310 315 320
 Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu
 325 330 335
 Ser Lys Met Leu Val Ile Asp Pro Ala Lys Arg Ile Ser Val Asp Asp
 340 345 350
 Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro Ala Glu Val
 355 360 365
 Glu Ala Pro Pro Pro Gln Ile Tyr Asp Lys Gln Leu Asp Glu Arg Glu
 370 375 380
 His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu Val Met Asn
 385 390 395 400
 Ser Glu Glu Lys Thr Lys Asn Gly Val Val Lys Gly Gln Pro Ser Pro
 405 410 415
 Ser Ala Gln Val Gln Gln
 420

<210> 2

<211> 340

<212> PRT

<213> Homo sapiens

<400> 2

Phe Tyr Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg
 1 5 10 15

Tyr Gln Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys
 20 25 30
 Ala Ala Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu
 35 40 45
 Ser Arg Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu
 50 55 60
 Leu Arg Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu
 65 70 75 80
 Asp Val Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr
 85 90 95
 Leu Val Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys
 100 105 110
 Gln Lys Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu
 115 120 125
 Arg Gly Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu
 130 135 140
 Lys Pro Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu
 145 150 155 160
 Asp Phe Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val
 165 170 175
 Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His
 180 185 190
 Tyr Asn Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu
 195 200 205
 Leu Leu Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln
 210 215 220
 Leu Lys Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu
 225 230 235 240
 Lys Lys Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr
 245 250 255
 Gln Met Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro
 260 265 270
 Leu Ala Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys
 275 280 285
 Arg Ile Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr
 290 295 300
 His Asp Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe
 305 310 315 320
 Glu Ser Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp

325

330

335

Glu Val Ile Ser
340

<210> 3

<211> 342

<212> PRT

<213> Homo sapiens

<400> 3

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Gly | Pro | Glu | Met | Val | Arg | Gly | Gln | Val | Phe | Asp | Val | Gly | Pro | Arg |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Tyr | Thr | Asn | Leu | Ser | Tyr | Ile | Gly | Glu | Gly | Ala | Tyr | Gly | Met | Val | Cys |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ser | Ala | Tyr | Asp | Asn | Val | Asn | Lys | Val | Arg | Val | Ala | Ile | Lys | Lys | Ile |
| | | | 35 | | | | 40 | | | | | 45 | | | |
| Ser | Pro | Phe | Glu | His | Gln | Thr | Tyr | Cys | Gln | Arg | Thr | Leu | Arg | Glu | Ile |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Lys | Ile | Leu | Leu | Arg | Phe | Arg | His | Glu | Asn | Ile | Ile | Gly | Ile | Asn | Asp |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | |
| Ile | Ile | Arg | Ala | Pro | Thr | Ile | Glu | Gln | Met | Lys | Asp | Val | Tyr | Ile | Val |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Gln | Asp | Leu | Met | Glu | Thr | Asp | Leu | Tyr | Lys | Leu | Leu | Lys | Thr | Gln | His |
| | | | 100 | | | | 105 | | | | | | 110 | | |
| Leu | Ser | Asn | Asp | His | Ile | Cys | Tyr | Phe | Leu | Tyr | Gln | Ile | Leu | Arg | Gly |
| | | | 115 | | | | 120 | | | | | 125 | | | |
| Leu | Lys | Tyr | Ile | His | Ser | Ala | Asn | Val | Leu | His | Arg | Asp | Leu | Lys | Pro |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Ser | Asn | Leu | Leu | Leu | Asn | Thr | Thr | Cys | Asp | Leu | Lys | Ile | Cys | Asp | Phe |
| 145 | | | | | 150 | | | | | 155 | | | | 160 | |
| Gly | Leu | Ala | Arg | Val | Ala | Asp | Pro | Asp | His | Asp | His | Thr | Gly | Phe | Leu |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Thr | Glu | Tyr | Val | Ala | Thr | Arg | Trp | Tyr | Arg | Ala | Pro | Glu | Ile | Met | Leu |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Asn | Ser | Lys | Gly | Tyr | Thr | Lys | Ser | Ile | Asp | Ile | Trp | Ser | Val | Gly | Cys |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Ile | Leu | Ala | Glu | Met | Leu | Ser | Asn | Arg | Pro | Ile | Phe | Pro | Gly | Lys | His |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Tyr | Leu | Asp | Gln | Leu | Lys | His | Ile | Leu | Gly | Ile | Leu | Gly | Ser | Pro | Ser |
| 225 | | | | | 230 | | | | | 235 | | | | 240 | |
| Gln | Glu | Asp | Leu | Asn | Cys | Ile | Ile | Asn | Leu | Lys | Ala | Arg | Asn | Tyr | Leu |

165

170

175

Lys Ala Val Asp Trp Trp Ala Leu Gly Val Leu Ile Tyr Glu Met Ala
 180 185 190

Ala Gly Tyr Pro Pro Phe Phe Ala Asp Gln Pro Ile Gln Ile Tyr Glu
 195 200 205

Lys Ile Val Ser Gly Lys Val Arg Phe Pro Ser His Phe Ser Ser Asp
 210 215 220

Leu Lys Asp Leu Leu Arg Asn Leu Leu Gln Val Asp Leu Thr Lys Arg
 225 230 235 240

Phe Gly Asn Leu Lys Asp Gly Val Asn Asp Ile Lys Asn His Lys Trp
 245 250 255

<210> 5

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 5

gctctagagc tccatgggca gcaaaagcaa agttgacaa

39

<210> 6

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 6

tagcggatcc tcattctgaa ttcattactt ccttgta

37

<210> 7

<211> 21

<212> PRT

<213> Homo sapiens

<400> 7

Lys Arg Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn
 1 5 10 15

Gln Ala Leu Leu Arg
 20